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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,813	02/26/2001	David Edwin Thurston	65435-9001	3683

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EXAMINER

WRIGHT, SONYA N

ART UNIT PAPER NUMBER

1626

DATE MAILED: 09/10/2002 8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/763,813

Applicant(s)

THURSTON ET AL.

Examiner

Sonya Wright

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 1-16 and 20-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 17-19 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) ✓ ✓ ✓
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3, 4, 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-26 are pending in this application.

Election/Restrictions

Applicant's election with traverse of Group II, claims 17-19 and the species of compound 51 in Fig. 11 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the claims of Groups I to IX form a single general inventive concept under PCT Rule 13.1 because under PCT Rule 13.2, they share special technical features. Applicant directs the Examiner's attention to the X'-Y-A- substituent. The Examiner has found Applicant's arguments persuasive, wherein Applicant submits that Takanabe et al. does not disclose the compounds of the present invention. However, Groups I to IX will not be rejoined because the claimed compounds are known in the art as disclosed by Thurston et al., Chemical Communications, 563-565 on page 563, compound 14, see the 102 rejection below. Thus the technical feature does not define a contribution which each of the claimed inventions, claimed as a whole, makes over the prior art.

The instant compound is generic to a plurality of patentably distinct species. The Examiner has generated a generic concept inclusive of the elected species. The following generic concept as depicted in claim 17 is identified for examination along with the elected embodiment: R2, R3, are as defined except that they are not X-Y-A; R6, R7, and R8 are as defined, except that in the group X-Y-A-, A is oxygen, and Y and Z are as defined; R9 is as defined. The remaining subject matter of claims 17-19 stands

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withdrawn from further consideration under 37 CFR 1.142(b) as constituting other patentably distinct inventions.

The withdrawn subject matter of claims 17-19 is properly restricted as said subject matter differs in structure and element from the elected subject matter so as to be patentably distinct therefrom, i.e. a reference which anticipated the elected subject matter would not even render obvious the withdrawn subject matter and fields of search are not co-extensive.

Claims 17-19 are objected to as containing non-elected subject matter. This objection may be overcome by limiting the claims to the elected subject matter identified supra.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Thurston et al, Chemical Communications, 563-565 (1996).

Applicant claims pyrrolobenzodiazepines which are useful as antitumour antibiotics. Thurston et al. teach pyrrolobenzodiazepine compounds which are useful as antitumour antibiotics. In Thurston et al., see page 563, column 1, first paragraph for the method of use, and see page 563, compound 14. The prior art teaches the instant claim when, in the instant claims, R2, R3, and R9 are hydrogen; R6 is hydrogen; R7 is OR wherein R is methyl; R8 is X-Y-A- defined as follows:

A is oxygen, Y is ethyl, Z is NHZ and Z is the nitrogen protecting group -C-EDTAEt3.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thurston et al, Chemical Communications, 563-565 (1996).

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicant claims pyrrolobenzodiazepines which are useful as antitumour antibiotics. Thurston et al. teach pyrrolobenzodiazepine compounds which are useful as antitumour antibiotics. In Thurston et al., see page 563, column 1, first paragraph for the method of use, and see page 563, compound 14. The prior art generically teaches the instant claims when, in the instant claims, R2, R3, and R9 are hydrogen or methyl; R6, R7, and R8 are OR, wherein R is alkyl or X-Y-A- defined as follows: A is oxygen, Y is alkyl, Z is NHZ and Z is the nitrogen protecting group -C-EDTAEt3.

The prior art teaches a specific example of the instant claims when R2, R3, and R9 are hydrogen; R6 is hydrogen; R7 is OR wherein R is methyl; R8 is X-Y-A- defined as follows: A is oxygen, Y is ethyl, Z is NHZ and Z is the nitrogen protecting group -C-EDTAEt3.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between Thurston et al. and the instant claims is that in the instant claims, X-Y-A can be in the R6, R7, or R8 position, while in Thurston et al. the X-Y-A group is in the position corresponding to R8 in the instant claims. Also, in the instant claims, the methoxy group can be in the R6, R7, or R8 position, while in Thurston et al. the methoxy group is in the position corresponding to R7 in the instant claims. Therefore, Thurston et al. teach positional isomers of the instant compound.

Further, in the instant claims, variables R2, R3, R9, and R6 can be hydrogen as well as alkyl, while in Thurston et al. the corresponding variables are hydrogen.

In the instant claims R and Y can be alkyl, while in Thurston et al. the corresponding variables are methyl and ethyl respectively.

Finding of prima facie obviousness---rational and motivation (MPEP §2142-2143)

However, nothing unobvious is seen in substituting the known claimed isomer for the structurally similar isomer, as taught by Thurston et al., since such structurally related compounds suggest one another and would be expected to share common properties absent a showing of unexpected results. In re Norris, 84 USPQ 458 (1950). One of ordinary skill in the art would be motivated to use the teachings of Thurston et al. to prepare the instant compounds in the expectation that positional isomers would be useful as antitumour antibiotics. Further motivation is provided because Thurston et al. teach a specific example of the instant compounds (supra).

Applicant defines that R2, R3, R9, and R6 can be alkyl while in Thurston et al., the corresponding variables are limited to hydrogen. However, it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137

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(C.C.P.A. 1978) and *In re Lohr*, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (ie., usefulness as an antitumour antibiotic).

Applicant defines R and Y to be alkyl, while in *Thurston et al.*, the corresponding variables are methyl and ethyl respectively. However, to those skilled in chemical art, one homolog is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. *In re Henze*, 85 USPQ 261 (1950). The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in the reference with the expectation of obtaining compounds which could be used as antitumour antibiotics. Therefore, the instant claimed compounds would have been suggested to one skilled in the art.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It appears that Applicant intends for claim 18 to be drawn to a method of use.

The preamble of claim 18 states that the claim is drawn to a compound while the rest of

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the claim is drawn to a method of use. If Applicant intends for the claim to be a method claim, the claim should be written in the proper form for a method of use claim.

Claim Objections

Claim 18 objected to under 37 CFR 1.75 as being a substantial duplicate of claim 17. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Applicant is advised that should claim 17 be found allowable, claim 18 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 17 is drawn to compounds of formula II. The preamble of claim 18 states that the claim is also drawn to compounds of formula II. Therefore, claims 17 and 18 are substantial duplicates.

Claims 17-19 are objected to because of the following informalities: Claim 17 depends on claims 2-8, which are non-elected claims. Claims 18 and 19 depend on claim 17, therefore they are also objected to. It is suggested that Applicant incorporate the subject matter of claims 2 to 8 into claim 17 in order to overcome the objection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sonya Wright, whose telephone number is (703) 308-4539. The examiner can normally be reached on Monday-Friday from 8:00 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (703) 308-4537. The Unofficial fax phone number for this Group is (703) 308-7922. The Official fax phone numbers for this Group are (703) 308-4556 or 305-3592.

When filing a FAX in Technology Center 1600, please indicate in the Header (upper right) "Official" for papers that are to be entered into the file, and "Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [joseph.mckane@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-1235.

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Joseph K. McKane

Supervisory Patent Examiner

Group 1600

Sonya Wright

September 4, 2002